

CLAIMS

What is claimed is:

1. A method comprising analyzing a sample containing a single molecule of interest in a resonant spectroscopic analysis chamber by a Raman spectroscopy.
2. The method of claim 1, wherein analyzing comprises analyzing with a stimulated Raman spectroscopy.
3. The method of claim 2, wherein analyzing comprises analyzing a sample containing a single nucleic acid derivative in solution.
4. The method of claim 3, further comprising identifying the nucleic acid derivative based on the analysis.
5. The method of claim 1:

wherein analyzing comprises analyzing in a micro-sized spectroscopic analysis chamber;

and

further comprising adding the sample to the chamber by flowing the sample into the chamber through a micro-sized fluid channel.
6. A method comprising:

adding a sample containing a molecule of interest in solution to a micro-sized resonant spectroscopic analysis chamber;

analyzing the sample with a resonance enhanced Raman spectroscopy by resonating inelastically scattered radiation within the chamber;

- identifying the sample based on the analysis.
7. The method of claim 6, wherein the molecule of interest comprises a single nucleic acid derivative.
 8. The method of claim 7, wherein analyzing comprises analyzing with a stimulated Raman spectroscopy.
 9. A method comprising:

irradiating a sample containing a single molecule of interest in a resonance chamber;

scattering radiation from the sample;

resonating the scattered radiation in the chamber;

irradiating the scattered radiation from the chamber; and

detecting the irradiated scattered radiation.
 10. The method of claim 9:

wherein scattering comprises inelastically scattering radiation from the molecule;

wherein resonating comprises reflecting the inelastically scattered radiation with a multi-layer dielectric mirror containing a layer having a thickness that is based on a wavelength of the inelastically scattered radiation for the molecule;

further comprising stimulating additional inelastically scattered radiation by irradiating the sample with the reflected inelastically scattered radiation; and

wherein irradiating the scattered radiation comprises transmitting the stimulated inelastically scattered radiation through a partial reflector.

11. The method of claim 10, wherein the single molecule of interest comprises a nucleic acid derivative.
12. The method of claim 9, further comprising stimulating additional inelastically scattered radiation by irradiating the sample with the resonated radiation.
13. The method of claim 9, wherein irradiating the sample comprises irradiating the sample with a first radiation having a first frequency with a second radiation having a second frequency.
14. The method of claim 9, further comprising identifying the sample based on the detected inelastically scattered radiation.
15. An analysis chamber comprising:

a resonant cavity to contain a sample for analysis;

at least one window to the cavity to transmit a first electromagnetic radiation having a first frequency into the cavity and to transmit a second electromagnetic radiation having a second frequency out of the cavity; and

a plurality of reflectors affixed to a housing of the cavity to reflect radiation of a predetermined frequency, the plurality of reflectors separated by a distance that is sufficient to resonate the radiation of the predetermined frequency.
16. The system of claim 15, wherein:

the cavity comprises a micro-sized cavity contained within a solid substrate;

the micro-sized cavity has a volume that is not greater than one microliter; and

the cavity is coupled with a micro-sized fluid channel to receive the sample for analysis.

17. The system of claim 15, wherein the at least one window comprises a partial reflector of the plurality of reflectors to transmit the second electromagnetic radiation out of the cavity.
18. The system of claim 15, wherein the plurality of reflectors comprises a reflector and a partial reflector, the reflector having a reflectivity for the first and second radiations that is greater than 99%, and the partial reflector having a reflectivity for the second radiation that is not greater than 99%.
19. The system of claim 15, wherein:

the plurality of reflectors comprise a multi-layer dielectric mirror; and

the second radiation comprises inelastically scattered Raman radiation.
20. The system of claim 15, further comprising the sample contained within the cavity, the sample containing a single nucleic acid derivative in solution, the nucleic acid derivative comprising a single base that is selected from the group consisting of adenine, cytosine, guanine, thymine, and uracil.
21. A spectroscopic analysis system comprising:

an electromagnetic radiation source to provide a first electromagnetic radiation;

a spectroscopic analysis chamber comprising:

a resonant cavity to contain a sample for analysis,

at least one window to the cavity to transmit the first electromagnetic radiation into the cavity and to transmit a second electromagnetic radiation out of the cavity, and

a plurality of reflectors affixed to a housing of the cavity to reflect radiation of a predetermined frequency, the plurality of reflectors separated by a distance that is sufficient to resonate the radiation of the predetermined frequency; and

an electromagnetic radiation detector to detect the second electromagnetic radiation.

22. The system of claim 21, wherein:

the first electromagnetic radiation comprises a radiation that is suitable for Raman spectroscopy;

the cavity comprises a micro-sized cavity, having a volume that is not greater than one microliter, contained within a solid substrate;

the cavity is coupled with a micro-sized fluid channel to receive the sample for analysis; and

the plurality of reflectors includes first multi-layer dielectric mirror having a reflectivity for the second radiation that is greater than 99% and a second multi-layer dielectric mirror having a reflectivity for the second radiation that is not greater than 99%; and

the second radiation comprises radiation having a frequency that has been shifted from a frequency of the first radiation based on an inelastic interaction with the sample.

23. The system of claim 21, further comprising a nucleic acid sequencing system containing the analysis system, the nucleic acid sequencing system comprising:

a sampling system to provide samples to the analysis system; and

a sample within the cavity, the sample containing a single nucleic acid derivative in solution, the nucleic acid derivative comprising a single base that is selected from the group consisting of adenine, cytosine, guanine, thymine, and uracil.

24. A method comprising analyzing a sample containing a single molecule of interest with a coherent Raman spectroscopy.
25. The method of claim 24, wherein the coherent Raman spectroscopy is selected from the group consisting of a stimulated Raman spectroscopy and a coherent anti-Stokes Raman spectroscopy.
26. The method of claim 24, wherein analyzing comprises analyzing a single nucleic acid derivative with a coherent anti-Stokes Raman spectroscopy.
27. The method of claim 26, wherein analyzing with the coherent anti-Stokes Raman spectroscopy comprises:

irradiating the nucleic acid derivative with a first radiation having a first wavelength and a second radiation having a second wavelength, wherein the first and the second radiation are substantially phase matched;

subsequently irradiating the nucleic acid derivative with a third radiation having the first wavelength; and

detecting a fourth radiation emitted by the nucleic acid derivative after irradiation with the third radiation, the fourth radiation containing a coherent beam having a predetermined direction and a third wavelength that is related to the first and the second wavelengths.

28. The method of claim 26, further comprising identifying the nucleic acid derivative based on the analysis.
29. The method of claim 27, further comprising geometrically separating the fourth radiation from the first and the second radiations.
30. The method of claim 29, wherein geometrically separating comprises irradiating the nucleic acid derivative with beams of the first, the second, and the third radiations from predetermined directions that allow photons of the beams to be combined according to momentum conservation to cause the nucleic acid derivative to emit photons in the predetermined direction.
31. A method comprising analyzing a sample containing a plurality of molecules of interest in a resonant spectroscopic analysis chamber by a Raman spectroscopy.
32. The method of claim 31, wherein analyzing includes analyzing the sample with a resonance enhanced Raman spectroscopy by resonating inelastically scattered radiation within the chamber.
33. The method of claim 32, wherein analyzing comprises analyzing with a stimulated Raman spectroscopy.
34. The method of claim 33, wherein the sample comprises a nucleic acid derivative.
35. The method of claim 34, further comprising identifying the nucleic acid derivative based on the analysis.